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09/403,967	03/28/2000	Bruno Guy	50019/006001	7903

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EXAMINER
PORTNER, VIRGINIA ALLEN

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1645	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/403,967	Applicant(s) Guy et al
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 4, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *29-58* is/are pending in the application.

4a) Of the above, claim(s) *29-38, 40-42, 45, and 58* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *39, 43, 44, and 46-57* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *29-58* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Claims 29-58 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group II, species 2, claims 39, 43 and 44 and generic claims generic: 46-57, in Paper No.12 is acknowledged.

2. Claims 29-38, 40-42, 45 and 58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups I and III, and non-elected species of Group II, specifically claims 40-42 and 45 there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 12.

Specification

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Drawings

4. Please insert a Brief Description of the Drawings.

Double Patenting

5. Claims 39, 50-51 and 57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,9-11,26 of U.S. Patent No. 6,126,938. Although the conflicting claims are not identical, they are not patentably distinct from each other because a genus claim is obvious over a species, wherein the agent used in the method of the instant invention is any Helicobacter agent, while agents of the issued method claims are limited to specific Helicobacter agents (see 6,126,938: claims, and col. 9, line 46).

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 recites a Markush group of compounds, each member being listed with a reference (I), (ii), or (iii). Member (ii) is the elected invention for examination. The number of compounds administered to a patient is only 1, which is defined through the recitation of the singluar of "compound" at line 3 of claim 39. The descriptive paragraph for Compound (ii) recites the phrase "said lipid is not provided in the form of a liposome when the composition does not comprise a saponin or a glycolipopeptide of formula (I). The word "composition" lacks antecedent basis in the claim because the immunogenic agent and the compound are not define to be apart of the same composition, but must only be administered to a patient. The "agent" and the "compound" are claimed in such a way that they may be administered sequentially or simultaneously. As no single composition is defined in the claims, the recited negative claim limitations are unclear because the Markush group does not define a composition that contains more than one compound, the agent and the compound are not defined to be in relationship one to the other and the claim is not directed to the administration of compositions that contain

multiple compounds. The recited negative limitation is not supported by the recited claim language because a combination composition that comprises both a saponin, and a cationic lipid or a glycolipopeptide and a cationic lipid is not supported by the recited claim language. The negative limitations allow the cationic lipid to be a liposome or a solution, the additional claim limitations directed to combination compositions containing a saponin or a glycolipopeptide are not encompassed by claim 39.

Claims 46-48 recite the phrase "wherein the T helper 1-type immune response is measured in mice". As mice will not be infected by all Helicobacter species, how can the patient of claim 39 be the mice of claim 46? Claim 39 defines the patient in the singular and claim 46 defines the patient to be in the plural "mice". As each mammal produces a different level of immune response when an immunogenic composition is administered, and the level is not always the same at any point in time after administration, it appears that the point in time a sample is taken in order to evaluate the immune response stimulated would be crucial to obtaining the claimed ratio of titers. (see Campbell, page 3, section 1.2.1 first paragraph and Laszlo et al (three patients received an immunogenic composition and the response differed). At what point after administration will the recited ratio exist?

Claims 46 and 47 define the titer induced to primarily be a Th-2 type immune response, while the preamble of the claim is directed to a method of stimulating a TH-1 immune response. IgG1 is indicative of a Th-2 immune response being stimulated; how can the method be a method of stimulating a Th-1 immune response when the major immune response being stimulated is a

Th-2 type immune response? What Helicobacter derived agent will induce the recited ratio of titers of T helper 1-type and T-helper type 2 immune response? The invention is not distinctly claimed based upon the fact that the agent is not specifically defined to be one that will induce a Th-1 type immune response.

Claims 46-48 are directed to the stimulation of both Th1 and Th2 immune response and the claimed method is directed to stimulating a Th1 immune response. Claim 46 stimulates a higher Th2 immune response by obtaining 20 times or more higher level of IgG1 (Th2 immune response) than IgG2a (Th1 immune response); claim 47 stimulates a higher TH2 immune response by obtaining 10 times higher level of IgG1 (Th2 immune response) than IgG2a (Th1 immune response); and claim 48 stimulates a higer Th2 immune response by obtaining 2 times or more IgG1 (Th2 immune response) than IgG2a (Th1 immune response). The recitation of "greater than or equal to" with respect to the recited ratios of IgG2a and IgG1 immune response defines an invention where the IgG1 immune response is preferred through the recitation of the phrase "greater than" and the IgG1 immune response is associated with a Th-2 immune response, not a Th-1 immune response as recited in the preamble. Are claims 46-48 directed to a different method from that of claim 39? Are Claims 46-48 directed to methods that stimulate immune responses based upon the ratio of immunoglobulins desired, rather than only a single type of immune response as set forth in the preamble of the independent claim ?

Claim Rejections - 35 U.S.C. § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Please Note: In light of the claims reciting unclear claim limitations in the Markush group, the elected compound is being read to include liposome or dispersion formulations. The phrase "under its diaphragm" is being read to include the region of the stomach that is situated under the diaphragm.

8. Claims 39, 44, 49-57 are rejected under 35 U.S.C. 102(e) as being anticipated by Guy et al (US Pat. 6,126,938, different inventive entity).

The claimed invention is directed to a method of inducing a T helper 1-type immune response against Helicobacter in a patient, the method comprising the step of administering an Helicobacter derived agent and a compound, wherein the elected compound is DC-chol* (a cationic lipid or salt thereof, *footnote cited references below).

Guy et al disclose a method of inducing a T helper 1-type immune (IgG2a immune response, see col. 8, lines 51, 62) response against Helicobacter in a patient (see col. 19, claim 1), the method comprising the step of administering an Helicobacter derived agent (see col. 8, lines

17-27, see claims 6-7 and 10-11) and a compound, wherein the elected compound is DC-chol (see col. 9, lines 45-46) (a cationic lipid or salt thereof).

The route of administration is taught to include pulmonary (strict systemic route, col. 6, line 9), nasal, buccal, stomach, intestine, urogenital, lungs, intragastric (see col. 6, lines 13-28), intradermal (see col. 9, line 31), intramuscular(col.9, line 28) and dorsolumbar region (see col5, lines 15-16 and col. 18, lines 43-52). The immunogenic agent and the compound were administered three times during treatment (see col. 9, lines 25-32, primary and two boosters).

Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guy et al, as applied to claims 39, 44, 49-57 above, in view of Epand et al (US Pat. 5,283,185).

The claimed invention is directed to a method of inducing a T helper 1-type immune response against Helicobacter in a patient, the method comprising the step of administering an

Helicobacter derived agent and a compound, wherein the elected compound is DC-chol*, formulated into a dispersion (a cationic lipid or salt thereof, *footnote cited references below).

See discussion of Guy et al above. The reference teaches, the agent to be a nucleic acid and/or an antigen, thus teaching the claimed method except the formulation of DC-chol into a dispersion for administration.

Epand et al teach DC-chol (see col. 14, claim 1) formulated into a dispersion(see col. 3, lines in an analogous art for the purpose of introducing a nucleic acid agent into cells.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the form of the compound used in the method of Guy et al to be the dispersion compound of DC-chol of Epand et al because the dispersion of Epand et al facilitates the transfer of DNA into cells (see col. 1, lines 1-8), the dispersion has weak protein kinase C inhibitory activity (see col. 2, lines 68), the dispersion is stable (see col. 3, lines 1-6 and Example XXVI).

The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of inducing a Th-1 immune response utilizing the agent of Guy et al and the dispersion compound of Epand et al because, both Guy et al and Epand et al teach the utilization of DC-chol as a compound in association with DNA for the delivery of the DNA to cells, and

Epand et al teaches advantages to the utilization of a dispersion with DNA for accomplishing the desired task of introducing DNA into cells, and Guy et al teaches upon introduction of the DNA agent into cells, the cells will induce an immune response.

In the absence of a showing of unexpected results, Guy et al in view of Epand et al, obviate the now claimed invention.

11. Claims 39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guy et al, as applied to claims 39, 44, 49-57 above, in view of Lockhoff et al (US Pat. 4,855,283).

The claimed invention is directed to a method of inducing a T helper 1-type immune response against Helicobacter in a patient, the method comprising the step of administering an Helicobacter derived agent and a compound, wherein the elected compound is DC-chol*, formulated into a dispersion (a cationic lipid or salt thereof, *footnote cited references below).

See discussion of Guy et al above. The reference teaches, the agent to be a nucleic acid and/or an antigen, thus teaching the claimed method except the formulation of the compound, into a dispersion for administration.

Lockhoff et al teach a compound of the formula (I) (see abstract) formulated into a dispersion (see suspension, col. 21, lines 14-15) together with an agent (antigen from a bacteria, col. 15,lines 42-60) in an analogous art for the purpose of inducing an immune response to the administered agent (Th-2), but also to potentiate an increase in the state of activity of macrophages (Th-1)(see col. 15, lines 23-27; lines 43-50).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the form of the compound used in the method of Guy et al to be the dispersion compound of Lockhoff et al because the dispersion of Lockhoff et al facilitates the stimulation of a Th-1 immune response, as well as an enhance Th-2 immune response, wherein the immune response is directed against the bacterial agent associated with the compound.

The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of inducing a Th-1 immune response utilizing the agent of Guy et al and the dispersion compound of Lockhoff et al because, Lockhoff et al teach the utilization of a compound that functions as a mitogen and stimulation of a Th-1 immune response (see Lockhoff et al, col. 15, line 21), as well as stimulates an enhanced immune response directed to the immunogenic agent administered in association with the compound dispersion (solution).

In the absence of a showing of unexpected results, Guy et al in view of Lockhoff et al, obviate the now claimed invention.

Conclusion

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

13.* US Pat. (5,283,185; 6,361,791 and 6,319,516) define DC-Chol to have the structural and functional characteristics recited in the claims of the instant invention (see claim 1 of 5,283,185).

14. Betbeder et al (US Pat. 6,096,291) is cited to show a method of stimulating a mucosal immune response utilizing an amphiphilic compound.

15. Della Valle et al (US Pat. 5,484,775) is cited to show the utilization of compounds that are aliphatic acids in inhibition of protein kinase C.

16. Illum et al (document number 2002/0025337) is cited to show lipid compounds for drug delivery.

17. Kelleher et al (document 2001/0010821) is cited to show H.pylori immunogenic compositions and antigens.

18. Lambert (US Pat. 5,900,246) is cited to show the utilization of lipophilic compounds in a drug delivery system.

19. Lockhoff et al (US Pat. 5,070,190) is cited to show compounds that stimulate phagocytosis (see col. 5, lines 61-62).

20. Malone et al (US Pat. 6,110,898) is cited to show DNA vaccines.

21. Marciani (US Pat. 6,080,725) is cited to show a saponin-lipophile in association with Helicobacter pylori antigens (see claims 1 and 12).

22. Nantz et al (US Pat. 5,824,812; 5,925,623; 5,892,071) are cited to show cationic transport compounds.

23. Schmitz et al (document number 2001/0041683) is cited to show cocoa sphingolipid compounds.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp

April 25, 2002

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